

**PLEASE CANCEL: CLAIMS 5, 17, 18 and 20.**

**PLEASE AMEND THE CLAIMS AS FOLLOWS:** namely,

1. (Withdrawn) A pharmaceutical composition for neuraxial delivery comprising both a hydrophilic N-linked glycosyl prodrug compound and a formulary, wherein said hydrophilic N-linked glycosyl prodrug compound comprises a CNS acting prodrug compound covalently linked with a saccharide through an amide or an amine bond and said formulary comprises an agent selected from the group consisting of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, an emollient, a disintegrant, a lubricating agent, an antimicrobial agent and a preservative, with the proviso that said saccharide moiety is not a cyclodextrin or a glucuronide.

2. (Withdrawn) The pharmaceutical composition of claim 1, further comprising a dosage form selected from the group consisting of a powder, a granule, an emollient cream, a tablet, a capsule, a lozenge, a trouch, a suppository, a perenteral solution, an injection solution, a syrup, an elixir, a nasal solution, an intrabronchial solution, an ophthalmic solution, a dermal patch and a bandage.

3. (Withdrawn) The pharmaceutical composition of claim 1, wherein said hydrophilic N-linked glycosyl prodrug compound further comprises a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises a CNS-acting prodrug compound; B, comprises a lower alkyl; D, comprises a nitrogen linker amine or amide; and, E comprises a saccharide, with the proviso that E is not a cyclodextrin or a glucuronide.

4. (Currently Amended) The method of claim 41 wherein said A-moiety is a CNS acting prodrug compound selected from the group consisting of ~~a stimulant, an anti-depressant, a neurotransmitter, a dopaminergic agent, a metabolic precursor compound, a muscle relaxant, a tranquilizer, an analgesic, a narcotic, a sedative, a hypnotic, a narcotic antagonist, a narcotic~~

~~analgesic, an anti-hypotensive agent, a  $\beta$ -blocker, an anti-hypertensive agent, a vasodilator, an anesthetic, an anti-epileptic compound, an anti-convulsant drug, a hormone, a sympatholytic agent, a centrally acting anti-cholinergic compound, a sympathetic stimulant, an adrenergic agent, a barbiturate antagonist, an anti-infective agent, an anticholinergic agent, an anticonvulsant, a sympatholytic, an ACE inhibitor, an anti-epilepsy agent, an antiviral agent, a gonadotropin synthesis stimulant, a diuretic and an emetic agent~~ chlorambucil, melphalan, acivicin, chlorambucil, uracil mustard, acetazolamide, L-Dopa, dopamine, histamine, amphetamine, dextroamphetamine, levamphetamine, aletamine, methamphetamine, phentermine, ephedrine, pseudoephedrine, phenylephrine, lidocaine and derivatives thereof.

5. (Canceled)

6. (Withdrawn) A process for preparing a hydrophilic N-linked glycosyl prodrug compound for neuraxial delivery, comprising the step of N-linking a CNS acting prodrug compound with a saccharide moiety under conditions suitable for formation of an amide or amine bond between said CNS acting prodrug compound and said saccharide moiety.

7. (Withdrawn) The process of claim 6, wherein said hydrophilic N-linked glycosyl prodrug compound comprises a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises said CNS-acting prodrug; B, comprises an optional lower alkyl; D, comprises said N-linker amine or amide; and, E comprises said saccharide, with the proviso that E is not a cyclodextrin or a glucuronide.

8. (Withdrawn) A process for preparing a pharmaceutical composition comprising hydrophilic N-linked glycosyl prodrug compound for neuraxial delivery, comprising the steps of N-linking a CNS acting prodrug compound with a saccharide moiety under conditions suitable for formation of an amide or amine bond between said CNS acting prodrug compound and said saccharide moiety; and formulating said N-linked glycosyl prodrug compound into said

pharmaceutical composition by addition of an agent selected from the group consisting of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, an emollient, a disintegrant, a lubricating agent, an antimicrobial agent and a preservative.

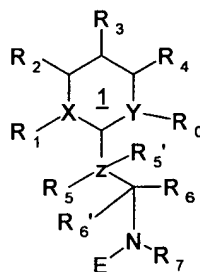
9. (Withdrawn) A method for treating a neurological dysfunction in a subject in need thereof comprising the step of administering to the subject a pharmaceutical composition comprising a compound according to FORMULA I:

A-B-D-E

Formula I

wherein, each of "-" comprises a single bond; A, comprises a CNS-acting prodrug; B, comprises a lower alkyl; D, comprises a nitrogen linker amine or amide; and, E comprises a saccharide, with the proviso that E is not a cyclodextrin.

10. (Currently Amended) The method of claim 41, wherein said CNS acting prodrug compound is a compound according to FORMULA IV,



Formula IV

wherein,

Ring 1 is a cyclic or heterocyclic ring, or aryl or heteroaryl ring, all of said rings comprising 4 to 8 carbon atoms, among which atoms are counted "X" and "Y";

R<sub>0</sub>, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are substituents of Ring 1;

either of X or Y is optional[[:]] and when present each of X and Y, ~~when present~~ is a carbon atom, a ~~halogen~~ nitrogen atom, a sulfur atom, an oxygen atom or a lower alkyl; and

E is a saccharide;

with the proviso that when E is a monosaccharide it is not a C<sub>6</sub> glucuronic acid and when E is an oligosaccharide it is not a cyclodextrin.

11. (Currently Amended) The method of claim 10, wherein said Ring 1 is an optionally substituted aryl or heteroaryl ring wherein if either one of X or Y ~~comprises~~ is a halogen nitrogen atom, a sulfur atom or an oxygen atom then the other of X or Y ~~comprises~~ is a carbon atom.

12. (Original) The method of claim 11, wherein said R<sub>2</sub> and R<sub>3</sub> are hydroxyl.

13. (Previously Presented) The method of claim 12, wherein said R<sub>1</sub> and R<sub>4</sub> are selected from the group consisting of hydrogen, hydroxyl, halogen, halo-lower alkyl, alkoxy, alkoxy-lower alkyl, halo-alkoxy, thioamido, amidosulfonyl, alkoxycarbonyl, carboxamide, amino-carbonyl and alkylamine-carbonyl.

14. (Previously Presented) The method of claim 10, wherein each of X and Y is an alkyl having 2 carbon atoms.

15. (Previously Presented) The method of claim 10, wherein each of X and Y is an alkyl having 1 carbon atom.

16. (Previously Presented) The method of claim 10, wherein Z is an alkyl having 1 or 2 carbon atoms.

17. (Canceled)

18. (Canceled)

19. (Previously Presented) The method of claim 10, wherein Z and R<sub>6</sub> is a carbonyl group, N is a nitrogen atom of an amide and R<sub>7</sub> is hydrogen.

20. (Canceled)

21. (Currently Amended) The method of claim 10, wherein said E substituent is selected from the group consisting of a radical of a monosaccharide, a disaccharide, a trisaccharide and an oligosaccharide.

22. (Previously Presented) The method of claim 10, wherein said E monosaccharide is a radical of a sugar selected from the group consisting of aldose, ketoaldose, alditols, ketoses, aldonic acids, ketoaldonic acids, aldaric acids, ketoaldaric acids, amino sugars, keto-amino sugars, uronic acids, ketouronic acids, lactones and keto-lactones.

23. (Currently Amended) The method of claim ~~22-41~~, wherein said ~~radical of a sugar~~ E monosaccharide is ~~further~~ selected from the group consisting of triosyl, tetraosyl, pentosyl, hexosyl, heptosyl, octosyl and nonosyl radicals.

24. (Previously Presented) The method of claim 23, wherein said pentosyl sugar radical is a straight carbon chain or a furanosyl ring.

25. (Previously Presented) The method of claim 23, wherein said hexosyl sugar radical is a straight carbon chain, a furanosyl ring or a pyranosyl ring.

26. (Previously Presented) The method of claim 23, wherein said hexosyl radical is further selected from the group consisting of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fructose, ribo-hexulose, arabino-hexulose and lyxo-hexulose.

27. (Previously Presented) The method of claim 23, wherein said pentosyl radical is further selected from the group consisting of ribose, arabinose, xylose, lyxose, ribulose and xylulose.

28. (Previously Presented) The method of claim 23, wherein said heptosyl residue is sedoheptulose.

29. (Previously Presented) The method of claim 23, wherein said nonosyl residue is N-acetylneuraminic acid, N-glycolylneuraminic acid and diacetylneuraminic acid.

30. (Previously Presented) The method of claim 26, wherein said compound is glucose, galactose or fructose.

31. (Previously Presented) The method of claim 21, wherein said disaccharide, trisaccharide and oligosaccharide is a sugar homopolymer or a sugar heteropolymer.

32. (Previously Presented) The method of claim 31, wherein said sugar homopolymer comprises a glycoside selected from the group consisting of erythran, threan, riban, arabinan, xylan, lyxan, allan, altran, glucan, mannan, gulan, idan, galactan, talan and fructan.

33. (Previously Presented) The method of claim 31, wherein said sugar heteropolymer further is a glycoside selected from the group consisting of erythroside, threoside, riboside, arabinoside, xyloside, lyxoside, alloside, altroside, glucoside, mannoside, guloside, idoside, galactoside, taloside and fructoside.

34. (Previously Presented) The method of claim 33, wherein said sugar heteropolymer is a glycoside metabolized in a mammal to a glucosyl or a galactosyl monosaccharide.

35. (Previously Presented) The method of claim 32, wherein said glycoside is a riban, an arabinan, a glucan, a galactan and a mannan.

36. (Previously Presented) The method of claim 33, wherein said glycoside is a riboside, an arabinoside, a glucoside, a galactoside, a mannoside and a fructoside.

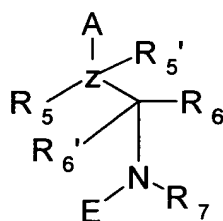
37. (Previously Presented) The method of claim 34, wherein said glucan is maltose, amylose, glycogen, cellobiose, amylopectin and heparin.

38. (Previously Presented) The method of claim 35, wherein said glucoside is sucrose.

39. (Previously Presented) The method of claim 35, wherein said fructoside is fucosidolactose.

40. (Previously Presented) The method of claim 35, wherein said galactoside is lactose, hyaluronic acid and pectin.

41. (Currently Amended) A method for simultaneously improving both the aqueous solubility and the blood brain barrier penetrability of a drug, comprising the steps of forming covalent linkages-single bonds between the drug, a bridging hydrocarbon moiety, a nitrogen atom of an amine or amide and a sugar or oligosaccharide and testing the reaction product for blood brain barrier penetrability by administering the reaction product to a test subject and measuring a brain penetration index, wherein the reaction product of said steps is a compound according to FORMULA I:



Formula I

wherein, ~~each of "-" is a single bond;~~ A[[.]] is a cyclic, heterocyclic, aryl or heteroaryl CNS-acting prodrug ~~selected from TABLE A or from TABLE B;~~

Z, R<sub>5</sub> and R<sub>5'</sub> are optional; when Z is present Z, R<sub>5</sub> and R<sub>5'</sub> together form is a lower alkyl having substituents R<sub>5</sub>, R<sub>5'</sub> or a substituted lower alkyl;

R<sub>6</sub> and R<sub>6'</sub> are substituents on a carbon atom linking Z with N through a single bond, or when Z is absent, linking N with Ring 1[[.]] and the carbon atom, R<sub>6</sub> and R<sub>6'</sub> together form a lower alkyl or a substituted lower alkyl;

N is a nitrogen atom of an amine or an amide linked with E through a single bond and having R<sub>7</sub> as a substituent; ~~and~~

E is a saccharide, with the proviso that when E is a monosaccharide it is not a C<sub>6</sub> glucuronic acid and when E is an oligosaccharide it is not a cyclodextrin[[.]];

wherein,

(i) said brain penetration index comprises determining the amount of drug in a brain sample and in a liver sample and calculating the brain penetration index by dividing the amount of the drug in the brain by the amount of drug in the liver; and,

(ii) said brain penetration index of the reaction product is about 2% to about 500%.

42. (Withdrawn) A method of treating a subject in need thereof to effect a metabolic replacement therapy, comprising the step of administering to said subject a therapeutic compound, wherein said therapeutic compound comprises a hydrophilic compound transportable intact by an intestinal glucose transporter, transportable intact in blood, transportable intact by endothelial cells at a blood brain barrier and metabolizable by a neuronal cell, wherein said therapeutic compound further comprises a compound binding to a dopamine receptor and metabolizable in said neuronal cell to effect said metabolic replacement therapy and said subject comprises a patient with a neurological dysfunction, a Parkinson's disease or a Parkinson's related disease.